

## Urine Culture Testing for Bacteria

Policy Number: AHS – G2156 – Urine Culture Testing for Bacteria	Prior Policy Name and Number, as applicable:
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### I. Policy Description

Bacteriuria is the presence of bacteria in the urine. Urinary tract infections (UTIs) can occur in the urinary system and can be either symptomatic or asymptomatic. UTIs can include cystitis, an infection of the bladder or lower urinary tract; pyelonephritis, an infection of the upper urinary tract or kidney; urosepsis; urethritis; and male-specific conditions, such as bacterial prostatitis and epididymitis (Bonkat et al., 2021; Hooton & Gupta, 2021). Typically, in an infected person, bacteriuria and pyuria (the presence of pus in the urine) are present and can be present in both symptomatic and asymptomatic UTIs. A urine culture can be performed to determine the presence of bacteria and to characterize the bacterial infection (Meyrier, 2019).

For guidance on pathogen panel testing from urine samples, please see AHS-G2149 Pathogen Panel Testing.

### II. Related Policies

Policy Number	Policy Title
AHS-G2149	Pathogen Panel Testing

### III. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request

1. In pregnant women, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) for any urinary tract infection, asymptomatic or symptomatic, including suspected cystitis, pyelonephritis, and asymptomatic bacteriuria **MEETS COVERAGE CRITERIA.**
2. For asymptomatic patients prior to undergoing urological interventions breaching the mucosa, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **MEETS COVERAGE CRITERIA.**
3. For patients exhibiting at least one sign or symptom of possible UTI or bacteriuria\* (See Note 1 below), urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **MEETS COVERAGE CRITERIA.**

4. To assess pyelonephritis, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **MEETS COVERAGE CRITERIA.**
5. For asymptomatic urinary tract infection or asymptomatic bacteriuria in all other instances, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **DOES NOT MEET COVERAGE CRITERIA.**
6. Follow-up urine culture testing for an uncomplicated urinary tract infection in patients that show evidence of clinical resolution of infection **DOES NOT MEET COVERAGE CRITERIA.**

*The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of a patient's illness.*

7. Urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **DOES NOT MEET COVERAGE CRITERIA** in the following situations:
  - a. As part of initial screening for asymptomatic prostatitis; OR
  - b. As part of assessment or prognosis of prostate biopsy

**\*NOTE 1:** Signs and symptoms of UTI/bacteriuria include (CDC, 2019)

- Fever
- Urgency to urinate
- Feeling the need to urinate despite having an empty bladder
- Increased frequency of urination
- Dysuria
- Suprapubic tenderness
- Pyuria
- Hematuria
- Cloudy urine
- Lower Back and Side (flank) pain
- Nausea
- Vomiting
- Chills
- Night sweats
- Pelvic pressure
- Change in urine smell
- Abnormal urinalysis findings

#### **IV. Scientific Background**

Urinary tract infections (UTIs) can be either symptomatic or asymptomatic and can also be classified as uncomplicated or complicated. Uncomplicated UTIs are “acute, sporadic or recurrent lower (uncomplicated cystitis) and/or upper...UTI, limited to non-pregnant, pre-menopausal women with no

known relevant anatomical and functional abnormalities within the urinary tract or comorbidities... All UTIs which are not defined as uncomplicated [are complicated UTIs]. Meaning in a narrower sense UTIs in a patient with an increased chance of a complicated course: i.e. all men, pregnant women, patients with relevant anatomical or functional abnormalities of the urinary tract, indwelling urinary catheters, renal diseases, and/or with other concomitant immunocompromising diseases for example, diabetes (Bonkat et al., 2021; Bonkat et al., 2018)". For complicated UTIs, *Escherichia coli* is the most common cause; however, "other uropathogens include other Enterobacteriaceae (such as *Klebsiella* spp and *Proteus* spp), *Pseudomonas*, enterococci, and staphylococci (methicillin-sensitive *Staphylococcus aureus* [MSSA] and methicillin-resistant *S. aureus* [MRSA])" (Hooton & Gupta, 2021). Even though both bacteriuria and pyuria are often present in UTIs, their presence alone is not indicative of a symptomatic infection.

The presence of bacteriuria does not guarantee negative outcomes for a patient. In fact, the paradigm of the sterility of the bladder environment has changed considerably over recent years. At least for females, the presence of female urinary microbiota (FUM) is believed to occur naturally and has been documented using sensitive bacterial DNA screening tests on asymptomatic females (Brubaker & Wolfe, 2016). Beneficial microbes, such as vaginal strains of *Lactobacillus*, can inhibit the growth of uropathogenic bacteria, including *E. coli* (Aroutcheva et al., 2001; Brubaker & Wolfe, 2016). Over-prescribing antibiotics, especially in cases of asymptomatic bacteriuria, can lead to both an eradication of beneficial bacterial flora and an emergence of antibiotic-resistant bacteria. Prescribing antibiotics as a prophylactic measure or in the instance of asymptomatic bacteriuria is detrimental because it is of limited value and can also increase incidences of drug-resistance. A study in 2002 by Harding and colleagues show that antibiotic treatment in diabetic women with asymptomatic bacteriuria did not result in a decrease of future symptomatic UTIs as compared to the control group; in fact, the experimental group had higher rates of adverse antimicrobial reactions (Harding, Zhanel, Nicolle, & Cheang, 2002). Even though the evidence-based guidelines by various societies, such as the EAU (Bonkat et al., 2021; Bonkat et al., 2018) and SHEA (SHEA, 2019), do not recommend performing urine testing or treatment for asymptomatic bacteriuria, inappropriate treatment is still occurring; in fact, one study by Cope and colleagues show that 32% of catheter-associated cases of asymptomatic bacteriuria and asymptomatic UTI received inappropriate treatment (Cope et al., 2009). The Antimicrobial Resistance Epidemiological Survey on Cystitis (ARESC) shows that up to 10.3% of *E. coli* in UTIs are "resistant to at least three different classes of antimicrobial agents" with ampicillin having the highest degree of resistance (48.3%). This is a large study of 4264 women from ten different countries to show that antibiotic-resistance is of international importance (Schito et al., 2009).

### *Analytical Validity*

Urinalysis (UA) to detect nitrite and leukocyte esterase to indicate the presence of bacteria is an accepted laboratory practice. One report, though, has shown that the use of nitrite has "a sensitivity of 3%, a specificity of 97%, and a negative predictive value of 55% (Cooper, Raeburn, Hamilton-Miller, & Brumfitt, 1992)". A 2004 meta-analysis study (Devillé et al., 2004) asserts that the "sensitivities of the combination of both tests vary between 68 and 88% in different patient groups, but positive test results have to be confirmed." They did note that the accuracy of the leukocyte esterase testing was higher in urology patients with a diagnostic odds ratio (DOR) of 276 as compared to the accuracy of nitrites (for example, in elderly patients DOR = 108).

Urine culture is considered a “gold standard” for detecting the presence of bacteria in urine (Graham & Galloway, 2001; Schmiemann, Kniehl, Gebhardt, Matejczyk, & Hummers-Pradier, 2010). That being said, “the interpretation of culture results can be considered as more of an art than a science. A urine culture result depends on so many variables, such as appropriate collection, transport, and the limits of the methods of detection. The reliability of single positive urine culture in diagnosing UTI is only 80%, rising to 90% if a repeat culture shows identical results (Graham & Galloway, 2001).” This is using the definition of bacteriuria as being  $10^5$  bacteria/ml of urine.

A potential future alternative to the urine culture could be multiplex PCR-based molecular testing, which Wojno et al. (2020) had found to be noninferior to urine culture for detection and identification of the bacteria. Agreement between the two testing methods was 90%, which exceeded the 85% noninferiority threshold. The multiplex PCR was also able to detect bacteria in 36% of symptomatic patients who had negative urine cultures and detected more polymicrobial infections than urine culture in a shorter amount of time (6 hours vs 48 hours for urine culture).

### *Clinical Validity and Utility*

A study in 2010 (Bruyere, d'Arcier, Boutin, & Haillot, 2010) using 353 patients undergoing prostate biopsy show that the routine use of obtaining a pre-operative urine culture is not clinically relevant to positive outcomes. “Of the 353 men, 12 had a pre-biopsy-positive bacterial culture and underwent prostate biopsy without any infections complication. Fifteen patients with a negative pre-biopsy culture developed a post-biopsy-positive bacterial culture, but remained asymptomatic without any treatment. Only four men from the group without pre-biopsy bacteriuria developed an infectious complication, requiring 3 weeks of antibiotic therapy.” Both experimental and control groups had similar rates of complication, suggesting “that routine urine bacterial culture before prostate biopsy is not useful when antibiotic prophylaxis and enema are performed.”

The method of obtaining the urine sample for culture testing is important. This is especially true for children. A 2017 study of 4808 acutely ill children demonstrated that there was modest agreement between the results obtained if the test was conducted by a research laboratory versus a health service laboratory; however, the method of obtaining the urine sample did have significance. The calculated areas under the receiver-operator curve (AUC) for UTI ranged from 0.75-0.86 if the sample was obtained using a clean-catch method versus AUC values of 0.65-0.79 if the sample was obtained using “nappy pad samples”. The authors conclusions were that urine cultures did not necessarily have to be sent to a research lab for testing, but that “primary care clinicians should try to obtain clean catch samples, even in very young children” (Birnie et al., 2017). A smaller study of 83 infants compared the use of urine obtained either via bladder catheterization or suprapubic aspiration (SPA) (Eliacik et al., 2016). All 83 infants had previously tested positive using urine culture samples obtained via bladder catheterization. Then, they had samples removed by SPA. The SPA samples were used in both urinalysis and urine culture testing, and “only 24 (28.9%) and 20 (24%) yielded positive urine culture and abnormal urinalysis data, respectively.” This indicates a 71.1% false-positive result rate if the urine sample is obtained using bladder catheterization. “In infants younger than 12 months, SPA is the best method to avoid bacterial contamination, showing better results than transurethral catheterization (Eliacik et al., 2016).”

Another study (Ducharme, Neilson, & Ginn, 2007) researched the use of either urine cultures and/or reagent test strips for use in diagnosing UTIs in elderly patients. The study consisted of 100 elderly patients with one group having no symptoms and non-infectious complaints and a second group “presenting with acute confusion, weakness or fever but no apparent urinary symptoms”. Their

results show that “of the 33 positive cultures, 10 had negative reagent strips. Thirteen of the 14 positive nitrite tests were culture positive for a specificity of 92.8% and a sensitivity of 36.1%. Positive cultures did not infer a diagnosis of UTI. Of the 67 positive reagent strips, 41 (61.2%) were associated with negative cultures.” They conclude that, “in the elderly, reagent testing is an unreliable method of identifying patients with positive blood cultures. Moreover, positive urine culture rates are only slightly higher in patients with vague symptoms attributable to UTI than they are in (asymptomatic) patients treated for non-urologic problems, which suggests that many positive cultures in elderly patients with non-focal systemic symptoms are false-positive tests reflecting asymptomatic bacteriuria and not UTIs (Ducharme et al., 2007).”

A study by Price and colleagues (Price et al., 2016) show that using an enhanced quantitative urine culture (EQUC) increased the detection of microorganisms in UTIs. This study consisted of 150 female patients using an initial UTI symptom assessment questionnaire to divide them into symptomatic and asymptomatic groups. Both sets underwent culture testing using both conventional urine culture testing and an EQUC method. “Compared to expanded-spectrum EQUC, standard urine culture missed 67% of uropathogens overall and 50% in participants with severe urinary symptoms. Thirty-six percent of participants with missed uropathogens reported no symptom resolution after treatment by standard urine culture results.” Their protocol resulted in an “84% uropathogen detection relative to 33% detection by standard urine culture”.

Cantey, Gaviria-Agudelo, McElvania TeKippe, and Doern (2015) evaluated the utility of a Gram stain relative to UA. In reviewing 312 pediatric patients with suspected UTIs who had urine cultures, UA, and Gram stain performed, the researchers concluded that the UA “has excellent negative predictive value that is not enhanced by urine Gram stain and that antibiotic selection did not vary based on the urine Gram stain result.” When compared to the urine Gram stain, the UA had equal sensitivity (97.3% vs 97.5%) and a higher specificity (85% vs 74%). This could allow the UA to take precedent as a test performed over the Gram stain due to its increased efficiency and lower cost.

Petty et al evaluated the risk factors and clinical outcomes of treating asymptomatic bacteriuria (ASB) in hospitalized patients. 2733 patients with ASB (defined as “positive urine culture without any documented signs or symptoms attributable to urinary tract infection”) were included. 2259 patients were treated with antibiotics for a mean of 7 days. Certain characteristics tended to correlate with ASB treatment, such as positive urinalysis (odds ratio [OR] = 2.83), leukocytosis (OR = 1.55), and dementia (OR = 1.57). However, treatment of ASB was found to be associated with longer duration of hospitalization after urine testing (4 vs 3 days; relative risk, 1.37), although no other differences in secondary outcomes were identified. The authors concluded that “hospitalized patients with ASB commonly receive inappropriate antibiotic therapy. Antibiotic treatment did not appear to be associated with improved outcomes; rather, treatment may be associated with longer duration of hospitalization after urine testing.” The authors also recommended stewardship efforts to reduce inappropriate treatment (Petty et al., 2019).

Coussement et al investigated the prevalence of asymptomatic bacteriuria among kidney transplant patients beyond two months post-transplant. The authors identified 500 post-transplant patients, of which 17 had asymptomatic bacteriuria (3.4%). Further, of the 76 patients that were 2-12 months post-transplant, only 1 had asymptomatic bacteriuria, and of the other 424 patients, 16 patients had asymptomatic bacteriuria. The authors concluded that the prevalence of asymptomatic bacteriuria past the second month of kidney transplant was low and that further studies were needed to ascertain the cost-effectiveness of the screen-and-treat strategy in this population (Coussement et al., 2019).

This finding regarding screening and treating AB was confirmed by Fontserè et al. (2021), who found that the “treatment of AB diminished the microbiological cure and increased the rates of microbiologic relapses and reinfections... treated AB patients showed a trend of developing symptomatic urinary tract infection in the following six months.”

## V. Guidelines and Recommendations

### 1. 2016 – 2019 Choosing Wisely (AAP, 2016; AAP & ASPN, 2018; AMDA, 2019; SHEA, 2019)

Choosing Wisely, an initiative by the American Board of Internal Medicine (ABIM) Foundation, consists of several national organizations representing medical specialists that write recommendations within their respective field to help choose care based on scientific evidence and to help reduce testing redundancy.

#### 2019 AMDA-The Society for Post-Acute and Long-Term Care Medicine (AMDA, 2019)

In 2019, the AMDA updated their earlier 2017 Choosing Wisely guideline concerning the use of urine cultures. Due to overuse of antibiotics and overtreatment of UTIs, they state “Don’t obtain urine tests until clinical criteria are met.” Since the urine culture would have a high likelihood of yielding a positive result in an otherwise asymptomatic case, this “contributes to the over-use of antibiotic therapy in this setting, leading to an increased risk of diarrhea or other adverse drug events, resistant organisms and infection due to *Clostridioides difficile*.” They also note that “the finding of asymptomatic bacteriuria may lead to an erroneous assumption that a UTI is the cause of an acute change of status, hence failing to detect or delaying the more timely detection of 5 signs and symptoms likely indicative of uncomplicated cystitis. These include dysuria, and one or more of the following: frequency, urgency, supra-pubic pain or gross hematuria”.

#### 2018 American Academy of Pediatrics-Section on Nephrology and the American Society of Pediatric Nephrology (AAP & ASPN, 2018)

The AAP Section on Nephrology and the ASPN issued a joint Choosing Wisely recommendation stating, “Avoid ordering follow-up urine cultures after treatment for an uncomplicated urinary tract infection (UTI) in patients that show evidence of clinical resolution of infection. Studies have shown that clinical resolution of infection is adequate for determining effectiveness of antibiotic therapy after treatment for a UTI.”

#### 2016 American Academy of Pediatrics (AAP, 2016)

The AAP updated their Choosing Wisely recommendation in 2016: “Avoid the use of surveillance cultures for the screening and treatment of asymptomatic bacteriuria.” There is no evidence that surveillance urine cultures or treatment of asymptomatic bacteriuria is beneficial. Surveillance cultures are costly and produce both false positive and false negative results. Treatment of asymptomatic bacteriuria is harmful and increases exposure to antibiotics, which is a risk factor for subsequent infections with a resistant organism. This also results in the overall use of antibiotics in the community and may lead to unnecessary imaging.”

#### 2019 Society for Healthcare Epidemiology of America (SHEA, 2019)

The SHEA recommendation in Choosing Wisely is more encompassing: “Don’t perform cultures (e.g. urine, blood, sputum cultures) or test for *C. difficile* unless patients have signs or symptoms of infection. Tests can be falsely positive leading to over diagnosis and overtreatment. Although important for diagnosing disease when used in patients with appropriate signs or symptoms, these tests often are positive when an infection is not present. For example, in the absence of signs or symptoms, a positive blood culture may represent contamination, a positive urine culture could represent asymptomatic bacteriuria, and a positive test for *C. difficile* could reflect colonization. There are no perfect tests for these or most infections. If these tests are used in patients with low likelihood of infection, they will result in more false positive tests than true positive results, which will lead to treating patients without infection and exposing them to risks of antibiotics without benefits of treating an infection.”

## 2. 2021 European Association of Urology (EAU) (Bonkat et al., 2021)

The EAU in 2021 released an update to their extensive 2020 guidelines concerning urological infections. With respect to **asymptomatic bacteriuria**, they state (all with a ‘Strong’ strength of rating), “Do not screen or treat asymptomatic bacteriuria in the following conditions:

- Women without risk factors;
- Patients with well-regulated diabetes mellitus;
- Post-menopausal women;
- Elderly institutionalised patients;
- Patients with dysfunctional and/or reconstructed lower urinary tracts;
- Patients with renal transplants;
- Patients prior to arthroplasty surgeries;
- Patients with recurrent urinary tract infections.”

They do recommend with a ‘Strong’ rating to “screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa” and a ‘Weak’ rating to “screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment.” They do recommend to “diagnose **recurrent UTI** by urine culture” with a ‘Strong’ rating. Please note that recurrent UTI indicates that the occurrences are symptomatic. It is further specified that “A urine culture must therefore be taken prior to such interventions”.

With respect to **uncomplicated cystitis**, they give a ‘Strong’ rating to only perform urine culture analysis “in the following situations:

- Suspected acute pyelonephritis;
- Symptoms that do not resolve or recur within four weeks after the completion of treatment;
- Women who present with atypical symptoms;

- Pregnant women.”

The EAU gives a ‘Weak’ recommendation to “use urine dipstick testing for diagnosis of acute uncomplicated cystitis.”

In cases of uncomplicated **pyelonephritis**, the EAU recommends with a ‘Strong’ rating to “perform urinalysis (e.g. using the dipstick method), including the assessment of white and red blood cells and nitrite, for routine diagnosis” and to “perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis.”

The EAU defines **complicated UTI** (cUTI) as occurring “in an individual in whom factors related to the host (e.g. underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g. obstruction, incomplete voiding due to detrusor muscle dysfunction) are believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.” Other factors associated with cUTIs include vesicoureteral reflux, recent history of instrumentation, UTI in males, pregnancy, and healthcare-associated infections. “Laboratory urine culture is the recommended method to determine the presence or absence of clinically significant bacteriuria in patients suspected of having a cUTI”.

For **catheter-associated UTIs** (CAUTI), the EAU recommends with ‘Strong’ ratings to “not carry out routine urine culture in asymptomatic catheterised patients”, to “not use pyuria as sole indicator for catheter-associated UTI”, and to “not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from catheter-associated UTI.”

In cases of **urethritis**, the EAU states that “Clinicians should always perform point-of-care diagnostics (e.g. Gram staining, first-void urine with microscopy, leukocyte esterase testing) if available to obtain objective evidence of urethral inflammation and to guide treatment...men who meet the criteria for urethritis should be tested for *C. trachomatis*, *M. genitalium* and *N. gonorrhoea* with nucleic acid amplification tests (NAAT), even if point-of-care tests are negative for gonorrhoeae...*N. gonorrhoeae* and chlamydia cultures are mainly to evaluate treatment failures and monitor developing resistance to current treatment.” With a ‘Strong’ rating, they recommend:

- “Perform a gram stain of urethral discharge or a urethral smear to preliminarily diagnose gonococcal urethritis.”
- “Perform a validated nucleic acid amplification tests on a first-void urine sample or urethral smear to prior to empirical treatment to diagnose chlamydial and gonococcal infections.”
- “Perform a urethral swab culture, prior to initiation of treatment, in patients with a positive NAAT for gonorrhoea to assess the antimicrobial resistance profile of the infective strain.”
- “Use a pathogen directed treatment based on local resistance data.”

For **urosepsis**, the EAU strongly recommends to “Take a urine culture and two sets of blood cultures before starting antimicrobial treatment.”

For the diagnosis and disease management of **bacterial prostatitis** (BP), the EAU recommends with a ‘Strong’ rating to “perform the Meares and Stamey 2- or 4-glass test in patients with [chronic bacterial



prostatitis (CBP)]”. They only give a ‘Weak’ rating in the use of the urine dipstick test and blood culture with a total blood count for acute bacterial prostatitis (ABP). They also give a ‘Weak’ rating to their recommendation to “not routinely perform microbiological analysis of the ejaculate alone to diagnose CBP”; however, they give a ‘Strong’ recommendation to “treat acute bacterial prostatitis according to the recommendations for complicated UTIs” where they recommend a laboratory urine culture.

The EAU’s recommendation in cases of suspected **acute infective epididymitis** (with a ‘Strong’ rating) is “to obtain a mid-stream urine and a first voided urine for pathogen identification by culture and nucleic acid amplification test.” It should be noted that, if the acute scrotal pain and/or swelling is due to suspected torsion, then a urine culture is not necessary. In that case, “urgent surgical exploration” is recommended instead.

### **3. 2016 World Health Organization (WHO, 2016)**

The *WHO recommendations on antenatal care for a positive pregnancy experience* in 2016 does include a recommendation to test for asymptomatic bacteriuria (ASB) in pregnant women. “Midstream urine culture is the recommended method for diagnosing asymptomatic bacteriuria (ASB) in pregnancy. In settings where urine culture is not available, the onsite midstream urine Gram-staining is recommended over the use of dipstick tests as the method for diagnosing ASB in pregnancy.” They do make note of the amount of time a urine culture takes (up to 7 days) but state that it is “the gold standard”. The concern of ASB in pregnancy is because “ASB is associated with an increased risk of preterm birth”.

### **4. 2014 Canadian Paediatric Society (CPS) (Robinson et al., 2020)**

In 2014, the CPS issued their position statement titled *Urinary tract infection in infants and children: Diagnosis and management* and reaffirmed their statement in 2020. Their recommendations are for children >2 months old. They recommend that “infants from two to 36 months of age with a fever of >39°C and no other source for fever on history or physical examination...should have urine collected for urinalysis. Unless this test is completely normal, they should then have urine collected by catheter or suprapubic aspirate [SPA] sent for culture.” Currently, CPS notes this statement as inapplicable for infants under 2 months of age.

If the child has been toilet-trained, then the urine sample can be collected midstream in lieu of the catheter. “Children with possible UTI who require antibiotic treatment immediately for other indications, such as suspected bacteremia, should have urine collected for urinalysis, microscopy, and culture.” Again, this sample should be obtained via either catheterization or SPA unless the child has been toilet-trained. They also state that “urine collection must occur before starting antibiotics because a single dose of an effective antibiotic rapidly sterilizes the urine.”

### **5. 2011 American Academy of Pediatrics (AAP) (Roberts, 2011)**

The AAP issued guidelines for UTIs in children 2 to 24 months of age in 2011, which were reaffirmed in 2016. With an “A” grade for evidence quality and a strong recommendation, they issued their Action Statement 1: “If a clinician decides that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial agent is administered; the specimen needs to be obtained through catheterization or SPA, because the diagnosis of UTI cannot be established reliably through culture of

urine collected in a bag.” For instances where the clinician believes that the febrile child does not warrant immediate antimicrobial therapy, the AAP in Action Statement 2 (strong recommendation; “A” grade of evidence) the following: (Action Statement 2a) “If the clinician determines the febrile infant to have a low likelihood of UTI [in Table below] then the clinical follow-up monitoring without testing is sufficient.” In Action Statement 2b, the AAP states: “If the clinician determines that the febrile infant is not in a low-risk group [in Table below], then there are 2 choices. Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis. Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results positive for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultures; if urinalysis of fresh (<1 hour since void) urine yields negative leukocyte esterase and nitrite test results, then it is reasonable to monitor the clinical course without initiating anti-microbial therapy, recognizing that negative urinalysis results do not rule out a UTI with certainty.” The table below from (Roberts, 2011) depicts the level of risk factors separated by gender.

Individual Risk Factors: Girls	Probability of UTI	No. of Factors Present
White race Age < 12 mo Temperature $\geq 39^{\circ}\text{C}$ Fever $\geq 2$ d Absence of another source of infection	$\leq 1\%$	No more than 1
	$\leq 2\%$	No more than 2

  

Individual Risk Factors: Boys	Probability of UTI	No. of Factors Present	
		Uncircumcised	Circumcised
Nonblack race Temperature $\geq 39^{\circ}\text{C}$ Fever > 24 h Absence of another source of infection	$\leq 1\%$	a	No more than 2
	$\leq 2\%$	None	No more than 3

**FIGURE 2**  
Probability of UTI Among Febrile Infant Girls<sup>28</sup> and Infant Boys<sup>30</sup> According to Number of Findings Present. <sup>a</sup>Probability of UTI exceeds 1% even with no risk factors other than being uncircumcised.

## 6. 2011 Canadian Urological Association (CUA) (Dason, Dason, & Kapoor, 2011)

The CUA *Guidelines for the diagnosis and management of recurrent urinary tract infection in women* contains an algorithm for a “female without a prior history of structural or functional abnormalities of the urinary tract presenting with 3 or more UTIs in 12 months” that requires a urine culture during a time when the patient is symptomatic followed by a urine culture two weeks after initiating treatment with sensitivity-adjusted antibiotics (Level 4 evidence, Grade C recommendation [Recommendation 2c]). In doing so, this “may aid in confirming the diagnosis of UTI, as well as guiding further specialist evaluation and management.” For recurrent uncomplicated UTI, “culture and sensitivity analysis should be performed at least once while the patient is symptomatic.... A midstream urine bacterial count of  $1 \times 10^5$  CFU/L should be considered a positive culture while the patient is symptomatic.” For patients that choose an option of ‘self-start antibiotic’ therapy, “it is not necessary to culture the urine after UTI self-diagnosis since there is a 86% to 92% concordance between self-diagnosis and urine culture in an appropriately selected patient population. Patients are advised to contact a health care provider if symptoms do not resolve within 48 hours for treatment based on culture and sensitivity.”

## 7. American Urological Association (AUA) (AUA, 2017; Averch et al., 2014; Lightner, Wymer, Sanchez, & Kavoussi, 2020; Wolf Jr et al., 2012)

The AUA issued a white paper in 2014 concerning CAUTIs. In the white paper, they refer to the use of the National Surgical Quality Improvement Program (NSQIP) definition of UTIs, which does

reference the use of urine culture. It should be noted, however, that this definition requires at least a minimum of one of the following symptoms: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness. They, too, refer to the 2009 IDSA guidelines concerning CAUTIs as well as those of the EAU. They state that there are “no consistent guidelines are available on how to obtain urine for culture from chronically catheterized patients, or what constitutes true urinary tract infection versus asymptomatic bacteriuria.” They make note of a study concerning the possible cost-effectiveness of the use of dipsticks to screen asymptomatic ICU patients for CAUTIs. They conclude, “however, as previously discussed, screening of asymptomatic patients may not be warranted, and treatment is usually not recommended in these cases” (Averch et al., 2014).

The AUA released guidelines for primary vesicoureteral reflux in children and recommend “Urinalysis for proteinuria and bacteriuria is recommended. If the urinalysis indicates infection, a urine culture and sensitivity is recommended”. The AUA also recommends urinalysis annually as part of the follow-up procedure (AUA, 2017).

The AUA published an update to their 2012 guideline on Urologic Procedures and Antimicrobial Prophylaxis, termed a “Best Practice Statement”.

The AUA recommends that “Prior to any urologic procedure, evaluation of a patient’s urinary tract symptoms suggestive of a UTI should include a simple dipstick, laboratory performed microscopy, and/or formal culture”.

The AUA also states that “Positive microscopy findings should be confirmed with a culture for antimicrobial sensitivities in the perioperative setting where the risk of an SSI is high and targeted antimicrobial treatment may be required. Urine culture should not be performed without an accompanying urine microscopy due to common sample contamination as well as bacterial colonization”. (Lightner et al., 2020)

## **8. National Institute for Health and Care Excellence (NICE) (NICE, 2015, 2018)**

NICE recommends against using dipstick testing to diagnose UTIs in adults with urinary catheters. However, NICE states that patients with a UTI not responding to initial antibiotic treatment should have a urine culture (NICE, 2015).

NICE also recommended the following populations of children for a urine culture:

- in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection
- in infants and children with a high to intermediate risk of serious illness
- in infants under 3 months
- in infants and children with a positive result for leukocyte esterase or nitrite
- in infants and children with recurrent UTI
- in infants and children with an infection that does not respond to treatment within 24–48 hours, if no sample has already been sent

- when clinical symptoms and dipstick tests do not correlate (NICE, 2018)
- 9. 2019 American Urological Association (AUA)/Canadian Urological Association (CUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) (Anger et al., 2019)**

These joint guidelines focus on “recurrent episodes of uncomplicated cystitis in women” and are not intended for “pregnant women, patients who are immunocompromised, those with anatomic or functional abnormalities of the urinary tract, women with rUTIs due to self-catheterization or indwelling catheters, or those exhibiting signs or symptoms of systemic bacteremia, such as fever and flank pain”. Their recommendations are listed below:

- “Clinicians should obtain urinalysis, urine culture and sensitivity with each symptomatic acute cystitis episode prior to initiating treatment in patients with rUTIs. (Moderate Recommendation; Evidence Level: Grade C)”
- “Clinicians should omit surveillance urine testing, including urine culture, in asymptomatic patients with rUTIs” (Moderate Recommendation; Evidence Level: Grade C)”

**10. Infectious Diseases Society of America (IDSA) (Nicolle et al., 2019)**

These guidelines were intended to update the 2005 IDSA guidelines. Their recommendations for asymptomatic bacteriuria (ASB) are as follows:

- “In infants and children, we recommend against screening for or treating asymptomatic bacteriuria”.
- “In healthy premenopausal, nonpregnant women or healthy postmenopausal women, we recommend against screening for or treating ASB”.
- “In pregnant women, we recommend screening for and treating ASB”.
- “In older, community-dwelling persons who are functionally impaired, we recommend against screening for or treating ASB”.
- “In older persons resident in long-term care facilities, we recommend against screening for or treating ASB”.
- “In patients with diabetes, we recommend against screening for or treating ASB”.
- “In renal transplant recipients who have had renal transplant surgery >1 month prior, we recommend against screening for or treating ASB”.
- “In patients with nonrenal solid organ transplant (SOT), we recommend against screening for or treating ASB”.
- “In patients with high-risk neutropenia (absolute neutrophil count <100 cells/mm<sup>3</sup>, ≥7 days’ duration following chemotherapy), we make no recommendation for or against screening for or treatment of ASB”.

- “In patients with spinal cord injury (SCI), we recommend against screening for or treating ASB”.
- “In patients with a short-term indwelling urethral catheter (<30 days), we recommend against screening for or treating ASB”.
- “In patients undergoing elective nonurologic surgery, we recommend against screening for or treating ASB”.
- “In patients who will undergo endoscopic urologic procedures associated with mucosal trauma, we recommend screening for and treating ASB prior to surgery”.

The guideline also states that it has been reviewed and endorsed by the following societies: “the Society of Healthcare Epidemiology of America, Pediatric Infectious Diseases Society, American College of Obstetrics and Gynecology, Association of Medical Microbiology and Infectious Diseases Canada, European Society of Clinical Microbiology and Infectious Diseases, European Association of Urology, and the American Urological Association” (Nicolle et al., 2019).

### **11. US Preventive Services Task Force (USPSTF, 2019)**

The USPSTF recommends screening for “asymptomatic bacteriuria using urine culture in pregnant persons”, but recommends against “screening for asymptomatic bacteriuria in nonpregnant adults” (USPSTF, 2019).

### **12. American Society of Transplantation Infectious Diseases (Goldman & Julian, 2019)**

These guidelines focus on UTIs within the kidney transplant (KT) population. The recommendations are listed below:

“We recommend against routinely collecting urine culture or treating bacteriuria in asymptomatic KT patients more than two months after KT”.

“If screening asymptomatic KT recipients any time in the post-transplant period and AB [asymptomatic bacteriuria] is found, a second urine culture (minimizing risk of contamination) should be collected and reviewed prior to decision about whether or not to treat AB. We strongly recommend observation without treatment of asymptomatic KT patients recipients who show clearance of the initial bacteriuria or development of different organism in the urine” (Goldman & Julian, 2019).

### **13. Canadian Task Force on Preventive Health Care (Moore et al., 2018)**

This guideline focuses on screening for asymptomatic bacteriuria during pregnancy.

“We recommend screening pregnant women once during the first trimester with urine culture for asymptomatic bacteriuria”, which applies to “pregnant women who are not experiencing symptoms of a urinary tract infection and are not at increased risk for asymptomatic bacteriuria.” However, the guideline remarks that this recommendation is “weak” with “very-low” quality of evidence (Moore et al., 2018).

## VI. State and Federal Regulations, as applicable

### A. FDA

Searches for “urinalysis” and “urine culture” yielded a combined 67 results on April 3, 2021 (FDA, 2021). Additionally, many labs have developed specific urine culture tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA ’88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

### B. CMS

NCD 190.12 Urine Culture, Bacterial <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=25&ncdver=1&bc=AABAAAAAAAAAA&>

## VII. Applicable CPT/HCPCS Procedure Codes

Code Number	Code Description
87077	Culture, bacterial; aerobic isolate, additional methods required for definitive identification, each isolate
87086	Culture, bacterial; quantitative colony count, urine
87088	Culture, bacterial; with isolation and presumptive identification of each isolate, urine
87140	Culture, typing; immunofluorescent method, each antiserum
87149	Culture, typing; identification by nucleic acid (DNA or RNA) probe, direct probe technique, per culture or isolate, each organism probed
87181	Susceptibility studies, antimicrobial agent; agar dilution method, per agent (eg, antibiotic gradient strip)
87147	Culture, typing; immunologic method, other than immunofluorescence (eg, agglutination grouping), per antiserum

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*Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.*

## VIII. Evidence-based Scientific References

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